

R  $\equiv$  EcoRI      P  $\equiv$  Pst I  
 H  $\equiv$  Hind III    N  $\equiv$  Nco I  
 B  $\equiv$  Bcl II      Y  $\equiv$  Eco RV

FIG.1

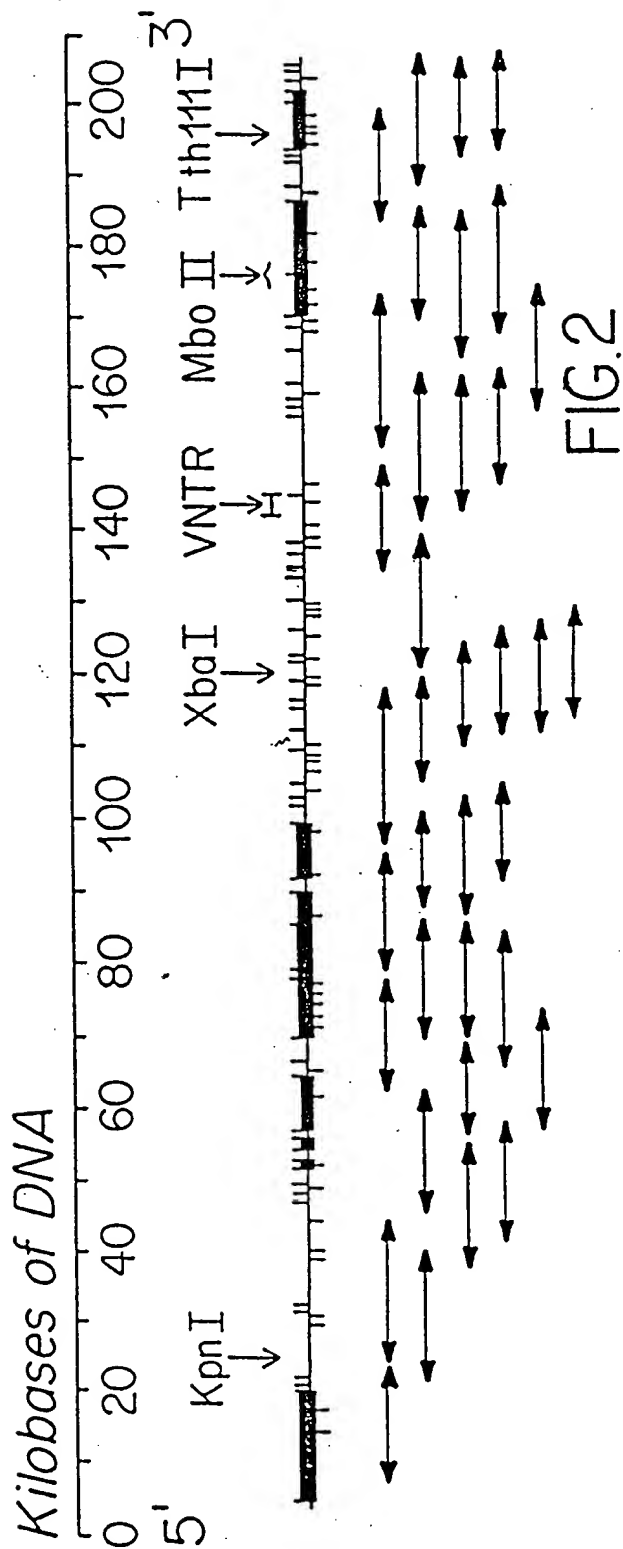
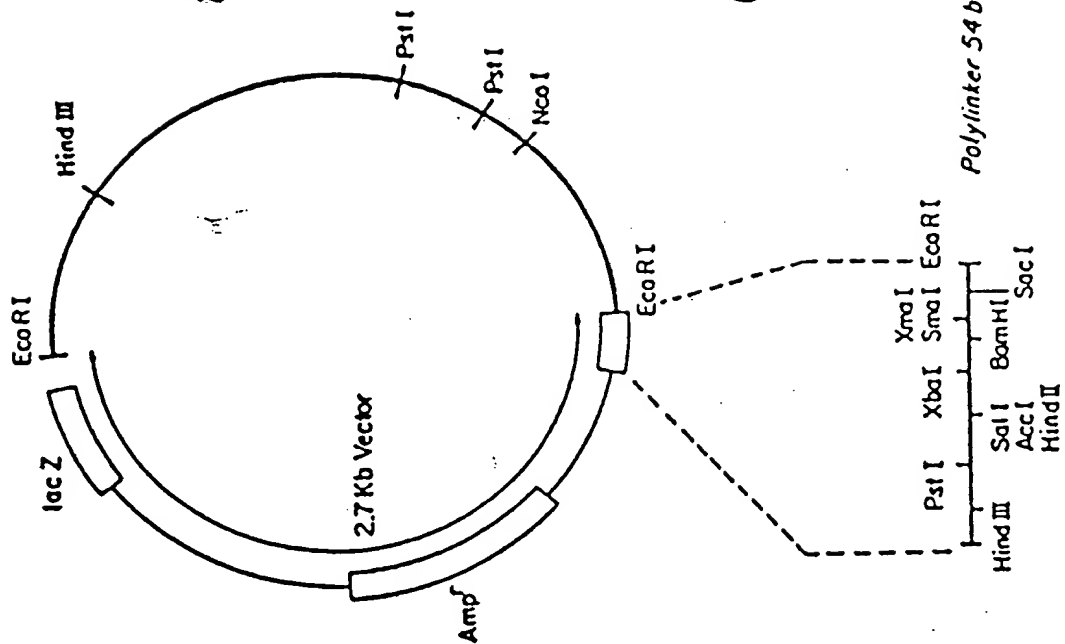


FIG.2

p2AR3.8

p3.8R in pUC13



p2AR0.9

p0.9R in pSP65

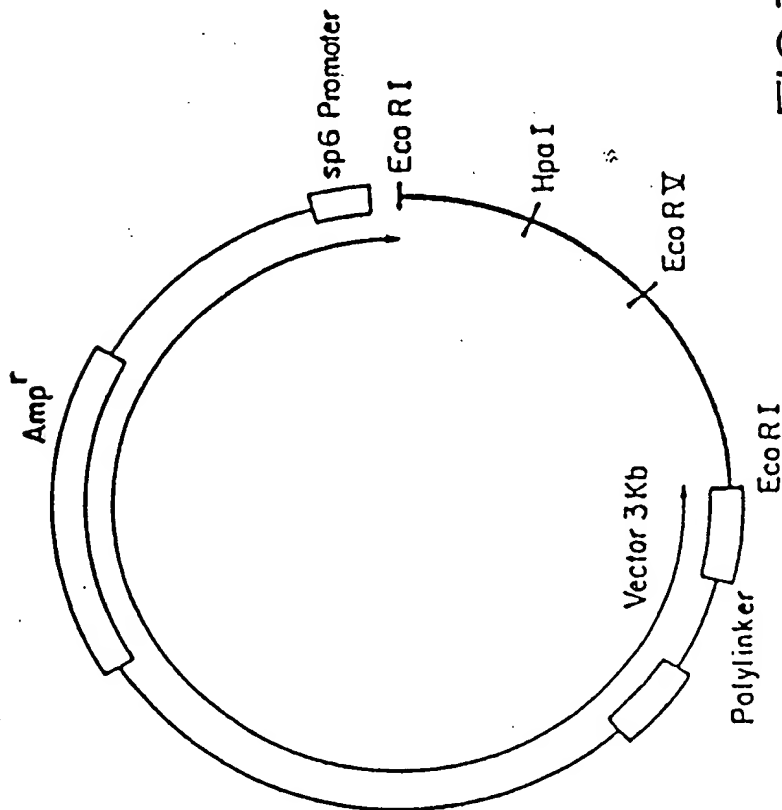


FIG.3

F-g. 4

# MAP OF THE RETINOBLASTOMA GENE

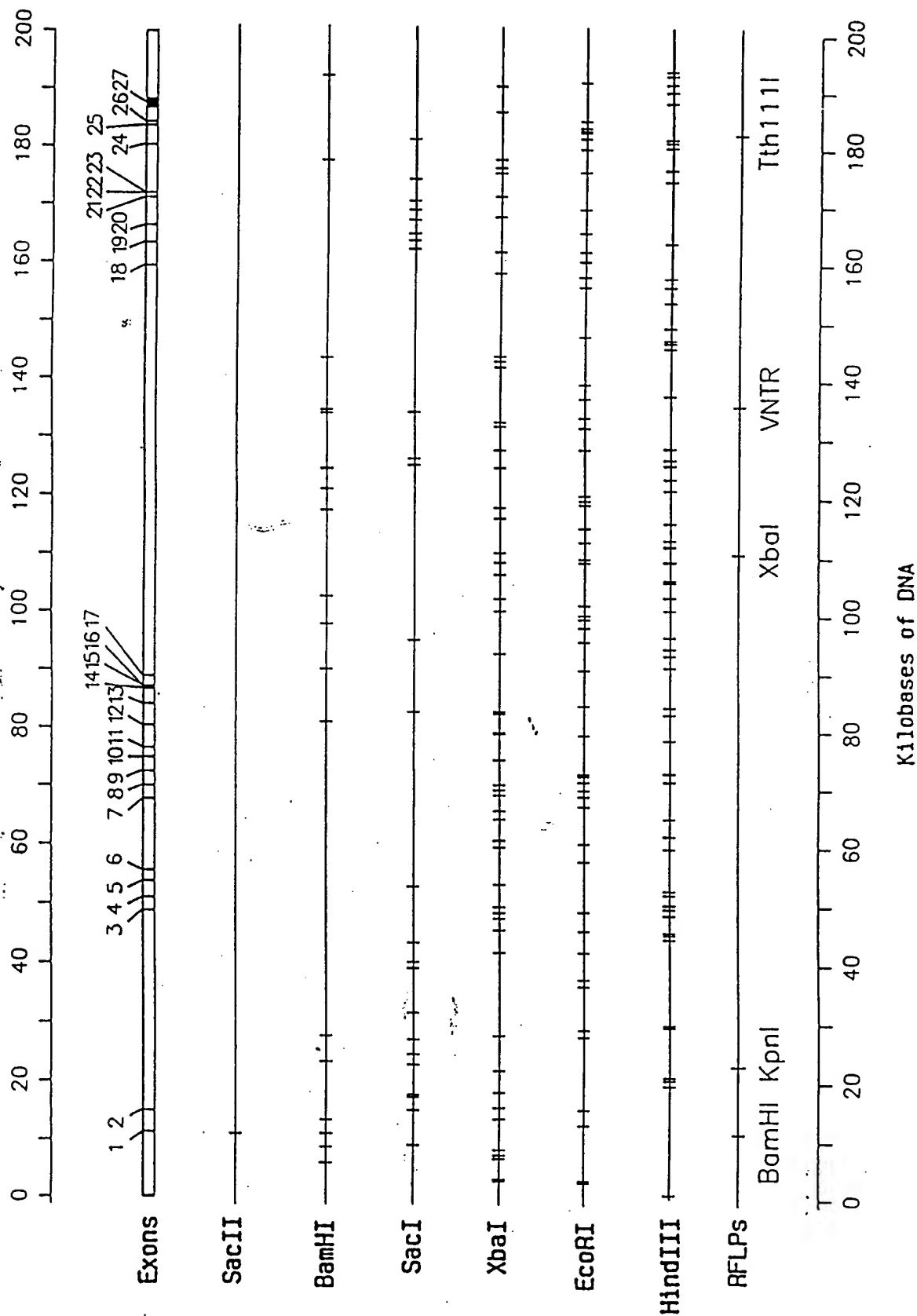


Fig. 5-1

GTCATGCCGCCCAAAACCCCCGAAAAACGGCCGCCACCGCCGCCGCTGCCGCCGCGGAACCCCCGGCACCGGCCGCCGC...80  
 CCCCTCCTGAGGAGACCAGAGCAGGACAGCGGCCCGGAGACCTGCCTCTCGTCAGGCTTGAGTTTGAAGAAACAGAAAG...160  
 AACCTGATTTTACTGCATTATGTCAGAAATTAAGATACCAGATCATGTCAGAGAGAGAGCTTGGTTAACTTGGGAGAAA...240  
 GTTTCATCTGTGGATGGAGTATTGGGAGGTTATATTCAAAGAAAAAGGAAGTGTGGGGAATCTGTATCTTTATTGCAGC...320  
 AGTTGACCTAGATGAG.....336

337	ATG TCG TTC ACT TTT ACT GAG CTA CAG AAA AAC ATA GAA ATC	378
	M S F T F T E L Q K N I E I	
379	AGT GTC CAT AAA TTC TTT AAC TTA CTA AAA GAA ATT GAT ACC	420
	S V H K F F N L L K E I D T	
421	AGT ACC AAA GTT GAT AAT GCT ATG TCA AGA CTG TTG AAG AAG	462
	S T K V D N A M S R L L K K	
463	TAT GAT GTA TTG TTT GCA CTC TTC AGC AAA TTG GAA AGG ACA	504
	Y D V L F A L F S K L E R T	
505	TGT GAA CTT ATA TAT TTG ACA CAA CCC AGC AGT TCG ATA TCT	546
	C E L I Y L T Q P S S S I S	
547	ACT GAA ATA AAT TCT GCA TTG GTG CTA AAA GTT TCT TGG ATC	588
	T E I N S A L V L K V S W I	
589	ACA TTT TTA TTA GCT AAA GGG GAA GTA TTA CAA ATG GAA GAT	630
	T F L L A K G E V L Q M E D	
631	GAT CTG GTG ATT TCA TTT CAG TTA ATG CTA TGT GTC CTT GAC	672
	D L V I S F Q L M L C V L D	
673	TAT TTT ATT AAA CTC TCA CCT CCC ATG TTG CTC AAA GAA CCA	714
	Y F I K L S P P M L L K E P	
715	TAT AAA ACA GCT GTT ATA CCC ATT AAT GGT TCA CCT CGA ACA	756
	Y K T A V I P I N G S P R T	
757	CCC AGG CGA GGT CAG AAC AGG AGT GCA CGG ATA GCA AAA CAA	798
	P R R G Q N R S A R I A K Q	
799	CTA GAA AAT GAT ACA AGA ATT ATT GAA GTT CTC TGT AAA GAA	840
	L E N D T R I I E V L C K E	
841	CAT GAA TGT AAT ATA GAT GAG GTG AAA AAT GTT TAT TTC AAA	882
	H E C N I D E V K N V Y F K	
883	AAT TTT ATA CCT TTT ATG AAT TCT CTT GGA CTT GTA ACA TCT	924
	N F I P F M N S L G L V T S	
925	AAT GGA CTT CCA GAG GTT GAA AAT CTT TCT AAA CGA TAC GAA	966
	N G L P E V E N L S K R Y E	
967	GAA ATT TAT CTT AAA AAT AAA GAT CTA GAT GCA AGA TTA TTT	1008
	E I Y L K N K D L D A R L F	
1009	TTG GAT CAT GAT AAA ACT CTT CAG ACT GAT TCT ATA GAC AGT	1050
	L D H D K T L Q T D S I D S	
1051	TTT GAA ACA CAG AGA ACA CCA CGA AAA AGT AAC CTT GAT GAA	1092
	F E T Q R T P R K S N L D E	
1093	GAG GTG AAT GTA ATT CCT CCA CAC ACT CCA GTT AGG ACT GTT	1134
	E V N V I P P H T P V R T V	
1135	ATG AAC ACT ATC CAA CAA TTA ATG ATG ATT TTA AAT TCA GCA	1176
	M N T I Q Q L M M I L N S A	
1177	AGT GAT CAA CCT TCA GAA AAT CTG ATT TCC TAT TTT AAC AAC	1218
	S D Q P S E N L I S Y F N N	

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Fig. 5-2

1219	TGC ACA GTG AAT CCA AAA GAA AGT ATA CTG AAA AGA GTG AAG	1260
	C T V N P K E S I L K R V K	
1261	GAT ATA GGA TAC ATC TTT AAA GAG AAA TTT GCT AAA GCT GTG	1302
	D I G Y I F K E K F A K A V	
1303	GGA CAG GGT TGT GTC GAA ATT GGA TCA CAG CGA TAC AAA CTT	1344
	G Q G C V E I G S Q R Y K L	
1345	GGA GTT CGC TTG TAT TAC CGA GTA ATG GAA TCC ATG CTT AAA	1386
	G V R L Y Y R V M E S M L K	
1387	TCA GAA GAA GAA CGA TTA TCC ATT CAA AAT TTT AGC AAA CTT	1428
	S E E E R L S I Q N F S K L	
1429	CTG AAT GAC AAC ATT TTT CAT ATG TCT TTA TTG GCG TGC GCT	1470
	L N D N I F H M S L L A C A	
1471	CTT GAG GTT GTA ATG GCC ACA TAT AGC AGA AGT ACA TCT CAG	1512
	L E V V M A T Y S R S T S Q	
1513	AAT CTT GAT TCT GGA ACA GAT TTG TCT TTC CCA TGG ATT CTG	1554
	N L D S G T D L S F p W I L	
1555	AAT GTG CTT AAT TTA AAA GCC TTT GAT TTT TAC AAA GTG ATC	1596
	N V L N L K A F D F Y K V I	
1597	GAA AGT TTT ATC AAA GCA GAA GGC AAC TTG ACA AGA GAA ATG	1638
	E S F I K A E G N L T R E M	
1639	ATA AAA CAT TTA GAA CGA TGT GAA CAT CGA ATC ATG GAA TCC	1680
	I K H L E R L E H R I M E S	
1681	CTT GCA TGG CTC TCA GAT TCA CCT TTA TTT GAT CTT ATT AAA	1722
	L A W L S D S P L F D L I K	
1723	CAA TCA AAG GAC CGA GAA GGA CCA ACT GAT CAC CTT GAA TCT	1764
	Q S K D R E G P T D H L E S	
1765	GCT TGT CCT CTT AAT CTT CCT CTC CAG AAT AAT CAC ACT GCA	1806
	A C P L N L P L Q N N H T A	
1807	GCA GAT ATG TAT CTT TCT CCT GTA AGA TCT CCA AAG AAA AAA	1848
	A D M Y L S P V R S P K K K	
1849	GGT TCA ACT ACG CGT GTA AAT TCT ACT GCA AAT GCA GAG ACA	1890
	G S T T R V N S T A N A E T	
1891	CAA GCA ACC TCA GCC TTC CAG ACC CAG AAG CCA TTG AAA TCT	1932
	Q A T S A F Q T Q K P L K S	
1933	ACC TCT CTT TCA CTG TTT TAT AAA AAA GTG TAT CGG CTA GCC	1974
	T S L S L F Y K K V Y R L A	
1975	TAT CTC CGG CTA AAT ACA CTT TGT GAA CGC CTT CTG TCT GAG	2016
	Y L R L N T L C E R L L S E	
2017	CAC CCA GAA TTA GAA CAT ATC ATC TGG ACC CTT TTC CAG CAC	2058
	H P E L E H I I W T L F Q H	
2059	ACC CTG CAG AAT GAG TAT GAA CTC ATG AGA GAC AGG CAT TTG	2100
	T L Q N E Y E L M R D R H L	
2101	GAC CAA ATT ATG ATG TGT TCC ATG TAT GGC ATA TGC AAA GTG	2142
	D Q I M M C S M Y G I C K V	
2143	AAG AAT ATA GAC CTT AAA TTC AAA ATC ATT GTA ACA GCA TAC	2184
	K N I D L K F K I I V T A Y	

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Fig. 5-3

2185	AAG GAT CTT CCT CAT GCT GTT CAG GAG ACA TTC AAA CGT GTT	2226
	K D L P H A V Q E T F K R V	
2227	TTG ATC AAA GAA GAG GAG TAT GAT TCT ATT ATA GTA TTC TAT	2268
	L I K E E E Y D S I I V F Y	
2269	AAC TCG GTC TTC ATG CAG AGA CTG AAA ACA AAT ATT TTG CAG	2310
	N S V F M Q R L K T N I L Q	
2311	TAT GCT TCC ACC AGG CCC CCT ACC TTG TCA CCA ATA CCT CAC	2352
	Y A S T R P P T L S P I P H	
2353	ATT CCT CGA AGC CCT TAC AAG TTT CCT AGT TCA CCC TTA CGG	2394
	I P R S P Y K F P S S P L R	
2395	ATT CCT GGA GGG AAC ATC TAT ATT TCA CCC CTG AAG AGT CCA	2436
	I P G G N I Y I S P L K S P	
2437	TAT AAA ATT TCA GAA GGT CTG CCA ACA CCA ACA AAA ATG ACT	2478
	Y K I S E G L P T P T K M T	
2479	CCA AGA TCA AGA ATC TTA GTA TCA ATT GGT GAA TCA TTC GGG	2520
	P R S R I L V S I G E S F G	
2521	ACT TCT GAG AAG TTC CAG AAA ATA AAT CAG ATG GTA TGT AAC	2562
	T S E K F Q K I N Q M V C N	
2563	AGC GAC CGT GTG CTC AAA AGA AGT GCT GAA GGA AGC AAC CCT	2604
	S D R V L K R S A E G S N P	
2605	CCT AAA CCA CTG AAA AAA CTA CGC TTT CAT ATT GAA GGA TCA	2646
	P K P L K K L R F D I E G S	
2647	GAT GAA GCA GAT GGA AGT AAA CAT CTC CCA GGA GAG TCC AAA	2688
	D E A D G S K H L P G E S K	
2689	TTT CAG CAG AAA CTG GCA GAA ATG ACT TCT ACT CGA ACA CGA	2730
	F Q Q K L A E M T S T R T R	
2731	ATG CAA AAG CAG AAA ATG AAT GAT AGC ATG GAT ACC TCA AAC	2772
	M Q K Q K M N D S M D T S N	
2773	AAG GAA GAG AAA	2784
	K E E K	

TGAGGATCTCAGGACCTTGGTGGACACTGTGTACACCTCTGGATTCTTGTCTCTCACAGATGTGACTGTATAACTTTCC 2864  
 CAGGTTCTGTTTATGGCCACATTTAATATCTTCAGCTCTTTTTGTGGATATAAAATGTGCAGATGCAATTGTTTGGGTGA 2944  
 TTCCTAAGCCACTTGAAATGTTAGTCATTGTTATTTATACAAAGATTGAAAATCTTGTGTAAATCCTGCCATTTAAAAAGT 3024  
 TGAGCAGATTGTTTCTCTTCCAAAGTAAATTTGCTGTGCTTTATGGATAGTAAGAATGGCCCTAGAGTGGGAGTCTCTG 3104  
 ATAACCCAGGCTGTCTGACTACTTTGCCTTCTTTGTAGCATATAGGTGATGTTTGCTCTTGTTTTATTAATTTATAT 3184  
 GTATATTTTTTAAATTTAATCATGAACACCCTTAGAAAATGTGTCCTATCTATCTTCCAAATGCAATTTGATTGACTGCC 3264  
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 AGCAAGTATAACCATATGATACTATCATACTACTGAAACAGATTTTCATACCTCAGAATGTAAAAGAATTTACTGATTAT 3504  
 TTTCTTCATCCAATTATGTTTTTAAATGAGGATTATTGATAGTACTCTTGGTTTTTATACCATTTCAGATCACTGAATTT 3584  
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 CAAGTGCACCTTTCTAATGTTTCTGGGCTCTGAAGAATTAAGATACAAATTAATTTTACTCCATAAACAGACTGTTAATTA 3744  
 TAGGAGCCTTAATTTTTTTTTCATAGAGATTGTCTAATTGCATCTCAAAATTTCTGCCCTCCTTAATTTGGGAAGGT 3824  
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 GTCAGTATGGTCAACACTGGCATGTTCAAAGCCACATTATTTCTAGTCCAAATTTACAAGTAATCAAGGGTCATTATGG 3984  
 GTTAGGCATTAATGTTTCTATCTGATTTTGTGCAAAAGCTTCAAAATTAACAGCTGCATTAGAAAAAGAGGCGCTTCTC 4064  
 CCTCCCTACACCTAAAGGTGATTTAACTATCTTGTGTGATTAATTTAGAGATGCTGTAACCTAAAAATAGGGG 4144  
 ATATTTAAGGTAGCTTCAGCTAGCTTTTAGGAAAAATCACTTTGTCTAACTCAGAATTATTTTAAAAAGAAATCTGGTCT 4224  
 TGTAGAAAAACAAATTTTATTTTGTCTCATTTAAGTTTCAAACTTACTATTTTGACAGTTATTTTGATAACAATGACA 4304  
 CTAGAAAACTTGACTCCATTTTCATCATTGTTTCTGCATGAATATCACAATCAGTTAGTTTTAGGTCAAGGGCTTAC 4384  
 TATTTCTGGGTCTTTTGTACTAAGTTTACATTAGAATTTAGTCCAGAATTTTAGGAACTTCAGAGATCGTGTATTGAGA 4464  
 TTTCTAAATAATGCTTCAGATATTATTGCTTTATTGCTTTTTTGTATTGGTTAAACTGTACATTTAAATTTGCTATGT 4544  
 TACTATTTTCTACAATTAATAGTTTGTCTATTTTAAATAAATTAGTTGTTAG..... 4597

Fig. 6-1

<u>SacII</u> EXON 1	aaggaggag	agtggngtcc	ngnngagggt	gcactagcca	gatattctgc	ggggcccgag	060
	agtcttccct	atcagacccc	gggataggga	tgaggcccac	AGTCACCCAC	CAGACTCTTT	120
	GTATAGCCCC	GTAAAGTGCA	CCCCGGCCTG	GAGGGGGTGG	TTCTGGGTAG	AAGCACGTCC	180
	GGGCCCGGCC	GGATGCCTCC	TGGAAGGCGC	CTGGACCCAC	GCCAGGTTTC	CCAGTTTAAT	240
	TCCTCATGAC	TTAGNGTCCC	AGCCNGCGCA	CCGACCAGCG	CCCCAGTTCC	CCACAGACGC	300
	CGGCGNGNNC	GGGAGCCTGC	GGACGTGAGC	GCGGGCGGAA	GTGACGTTTT	CCGCGGTTGG	360
	ACGCGCGCCT	CAGTTGCCGG	GCGGGGGAGG	GCGCGTCCGG	TTTTTCTCAG	GGGACGTTGA	420
	start of cDNA sequence						
	AATTATTTTT	GTAACGGGAG	TCGGGAGAGG	ACGGGGCGTG	CCCCGCGTGC	GCGCGCGTGC	480
	TCCTCCCCGG	CGCTCCTCCA	CAGCTCGCTG	GCTCCCGCGG	CGGAAAGGCG	TCATGCCGCC	540
<u>SacII</u>	CAAAACCCCC	CGAAAAACGG	CGCCACCCGC	CGCGCTGCC	GCCGCGGAAC	CCCCGGCACC	600
	oLysThrPro	ArgLysThrA	laAlaThrAl	aAlaAlaAla	AlaAlaGluP	roProAlaPr	(23)
	GCCGCGCGCG	CCCCCTCCTG	AGGAGGACCC	AGAGCAGGAC	AGCGGCCCGG	AGGACCTGCC	660
	oProProPro	ProProProG	luGluAspPr	oGluGlnAsp	SerGlyProG	luAspLeuPr	(43)
	TCTCGTCAGG	TGAGCGAGCA	GAGCGCGTCN	CTCACGCGGG	AAGGGCGCCC	CGGGTGTGCG	720
	oLeuValAr						(46)
	TAGGGCGGGC	GCAAGGCGgC	TCGGCGGGGA	CCCGTCCTCG	CCAGGGgCCG	GGTCCgGNG	780
	GGAGGAGGGC	CCCTCCCTGC	CCCCGCCAC	GGcggaGCGT	CTGCAGAATG	GTGACAGGAT	840
	TCTGGGTCTT	TGGGCGAGGG	GTCTCGGCTT	CAACTTGACA	GGTGTGGGGC	GGGTggggt	900
	agnntectga	gcgaagtgc	aggtgcagtt	ccctettgtg	agnctcggan	ncagaggntc	960
EXON 2	ggttgcgagcg	tncatcagac	aaaaaaatga	aaaaataaaa	tacaaaaa		1008
	--2.9 kb--						
	cccaaacagc	tttagctatt	acatttactt	tccttcacag	aagtgttttg	ctgctttgaa	060
	gatatttgac	ttaccatgca	agcaaatatt	tttcaactgtg	tggtatcctt	attttggaat	120
	gaccatgaaa	aagataatca	tatgnnnaaa	tttgaagtgt	aatgtttttc	taagataaaa	180
	taagatctta	AAGTATTTAA	TAATGTTCTT	TTTCACAGTA	GTGTTATGTG	CAAACATTATG	240
	AAACAAGTAT	GTAAGAATC	AATTTGATTT	ATAAGATATG	CCAATTATAT	GATTATTTTC	300
	ATTTGGTAGG	CTTGAGTTTG	AAGAAACAGA	AGAACCCTGAT	TTTACTGCAT	TATGTCAGAA	360
	gLeuGluPheG	luGluThrGl	uGluProAsp	PheActAlaL	euCysGlnLy		(63)
	ATTAAAGATA	CCAGATCATG	TCAGAGAGAG	AGCTTGTTTA	ACTTGGGAGA	AAGTTTCATC	420
<u>SacI</u>	sLeuLysIle	ProAspHisV	alArgGluAr	gAlaTrpLeu	ThrTrpGluL	ysValSerSe	(83)
	TGTGGATGGA	GTATTGGTAA	GGATTTTCTT	AAAACGTTTT	GAAATTTTTT	TTTCTCATTT	480
	rValAspGly	ValLeu					(88)
	TAAAACCAAC	TTCAAAATCAC	TATACAAAAA	TTGAAAGATA	GAAAAATATA	AAGACAATAA	540
	AAGctaataa	taattccatt	acccagagga	aatttacctc	tgctaacatt	aaaaatgttt	600
	gaggccgggc	acgtgggtca	tgccgtgaat	cctaccactt	tgggaggctg	aggcagggtg	660
	attgcctgag	ctcaggagtt	cgagaccagc	ctgggcaaca	tggt		704
	--33 kb--						
	ctatttgaga	tgactgaccc	ctaaagtctc	acaataacta	tttaattttt	tatcttttcta	060
	atactttttt	gccttataat	ataaaatttg	aatgtttgtt	attagtgtga	aatgaaatcc	120
EXON 3	tttcaaata	atgccatcag	aaggatgtgt	tacaaatata	cagtATTACA	AACATTATT	180
	TTGTATGCTG	AATAAGAAAA	AATCAGTTAT	AATACAGTTT	TAACATAGTA	TCCAGTGTGT	240
	GAATTATTTA	ATGAAATATT	TGATCTTTAT	TTTTTGTTCC	AGGGAGGTTA	TATTCAAAAG	300
					GlyGlyTy	rIleGlnLys	(94)
	AAAAAGGAAC	TGTGGGGAAT	CTGTATCTTT	ATTGCAGCAG	TTGACCTAGA	TGAGATGTGC	360
	LysLysGluL	euTrpGlyI1	eCysIlePhe	IleAlaAlaV	alAspLeuAs	pGluMetSer	(114)
	TTCACTTTTA	CTGAGCTACA	GAAAAACATA	GAAATCAGGT	AAAGTTTCTT	GTATAAATAT	420
	PheThrPheT	hrGluLeuG1	nLysAsnIle	GluIleSe			(127)
	AAGCCTCTGC	CATAAAAGGA	AACGAATTCT	GGATTTTCTT	CTCAATAGAC	TTTTGTGAAT	480
	TAGTGAGAAA	TGCTAAAATA	AAGTAAAACA	AAAAGAACTT	GGACCAATA	GTGAAGTCCC	540
<u>EcoRI</u>	ATTCTCTCAT	GGAGCCGTTA	TGAAAGTGTA	TTTATGCTGT	ATTTCTTTAA	GAGGTAGCAG	600
	TTTGTGTCCT	GGAAAAATTT	TCATTGTGTC	TCTCACTATT	CATGTGTAAG	C	651
--1.6 kb--							

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Fig. 6-2

EXON 4

gcataaggat atagataata gaggtgtaag ttgaaggcta attattttttg caaaaagtaa 060  
 ttccttccaa aggatatagt agtgatttga ttagagctg ataattttt GAATTGAAAT 120  
 ATCTATGATT TGAAAACGAA ATAACACAAA TTTTAAAGGT TACTGATTTA CTTTTTCTA 180  
 TTCTTTCCTT TGTAGTGTC ATAAATTCTT TAACTTACTA AAAGAAATTG ATACCACTAC 240  
                   rValH isLysPhePh eAsnLeuLeu LysGluIleA spThrSerTh (142)  
 CAAAGTTGAT AATGCTATGT CAAGACTGTT GAAGAAGTAT GATGTATTGT TTGCACTCTT 300  
 rLysValAsp AsnAlaMetS erArgLeuLe uLysLysTyr AspValLeuP heAlaLeuPh (162)  
 CAGCAAATTG GAAAGGTAAA GTAAACATTT TATTAGGGTT ACACTCTGAT TTTTATGTC 360  
 eSerLysLeu GluAr  
 ATTGTTTACA ATTAGATTCT GGAATTATT TAACACATTT AGTAAAGTTA GTAAGTATTA (167)  
 ATTCTTAGac ttgtcccttt taatgttagc tcattaattc ttagctttct tatttatcca 420  
 gtaa'atgca ttctgaatgc ttctggaag attaacggtt attatccttt catgtctcca 480  
 tttgttttca aaacttagct tategagtat  
                   --2.1 kb-- 570

EXON 5

gagatattta aagagnaact ttactaacct taggtggatc agctgggtgt tttctatctt 060  
 atttatacct tttttttgaa GACTAATTGA GAGGATTAAAC TGTAATTATA TATTAAAGTG 120  
 ATGTGAGATG TCATAAATTG GGAAATCTA CTTGAACCTT GTTTTATAAT GCTATATATT 180  
 TTTTGTTTT AAAATATATA CTCTTAAAA GAAGATGAAT AAAGCATGAG AAAACTACTA 240  
 TGACTTCTAA ATTACGAAAA AATGTTAAAA AGTCATAATG TTTTCTTTT CAGGACATGT 300  
                   gThrCys (169)  
 GAACTTATAT ATTTGACACA ACCCAGCAGT TCGTAAGTAG TTCACAGAAT GTTATTTTTC 360  
 GluLeuIleT yrLeuThrGl nProSerSer Se (180)  
 ACTTAAAAAA AAAGATTTT ATGAATAAT CTCAAACATC TTGATAGTTA GGGTTAGTTT 420  
 GATCGATTAT AGCAGGCTAC Ttcataaatt aagcccatag atttaagtc tgtgtagatt 480  
 atttatcttc tcacaaagaa aatagtataa aatacatgcc ttgtactaca aagaagaact 540  
 aataagggtg aattgattca ggacagcata tcaccaactc tgagaaaaat gcaacaaatg 600  
 caaattcatt gactaa  
                   --1.4 kb-- 616

EXON 6

aaatggactg cattctatta tgcatttaac taagggtcatt ttttttttaa tGCACAAAAA 060  
 GAAACACCCA AAAGATATAT CTGGAAGAACT TTCTTTCAGT GATACATTTT TCCTGTTTTT 120  
 TTTCTGCTTT CTATTGTTT AATAGGATAT CTACTGAAAT AAATTCTGCA TTGGTGCTAA 180  
                   rIleS erThrGluI1 eAsnSerAla LeuValLeuL (192)  
 AAGTTTCTTG GATCACATTT TTATTAGCTA AAGGTAAGTT CATTATATTT ATTAAATGCT 240  
 ysValSerTr pIleThrPhe LeuLeuAlaL ysG (203)  
 AATATTTCAA ATGTAATAAT TAAATTGGCA TTCCTTTGGA CTAAATCCCT CAATTTTAT 300  
 TGAGTAATGT ACTCCTccct cattctctgc ttggcttatt aactgttagc aagttcctat 360  
 aattctggtg ctagaacaaa ccttggaat gctttattta atntttgtt ctaatatcc 420  
 atcttccctc cctt  
                   --11.5 kb-- 434

EXON 7

tttatagtg ttttagacat aaagaattaa ttataacaga aatagcttaa atgtaaaatt 060  
 ctcagagtag agcttaacac ttgatttata attccataac tttacatatt tCTATTTTAC 120  
 ATATTTTATA CCTTTTAAAA CAGATTTTTT TTTTTTTTAC AAAAAAAGA AAGAAAATCT 180  
 TTACCATGCT GATAGTGATT GTTGAATGAA TAAATTTATG GATATACTCT ACCCTGCGAT 240  
 TTTCTCTCAT ACAAAGATCT GAATCTCTAA CTTCCTTTAA AAATGTACAT TTTTTTTTCA 300  
 GGGGAAGTAT TACAAATGGA AGATGATCTG GTGATTTTCA TTCAGTTAAT GCTATGTGTC 360  
 lyGluValL euGlnMetGl uAspAspLeu ValIleSerP heGlnLeuMa tLeuCysVal (222)  
 CTGACTATT TTATTAACT CTCACCTCCC ATGTTGCTCA AAGAACCATA TAGTAAGTAT 420  
 LeuAspTyrP heIleLysLe uSerProPro MetLeuLeuL ysGluProTy rL (240)  
 TTAATTTATG CCCCTTTTAC TTTCTCATTC AGCAGTTGCT TATTGAATGT CTAGTGGGTA 480  
 CCAAACATGG TTCTAAGGCT GACAGGATGA TAAAAAATAA ATCAgacatg gactttgccc 540  
 ataagtagtg taagttatag aaggaaagat aagacatgga acaaatgat tagagtatat 600  
 ggtagaaagt ggtttcgggt caaaatacaa caaatggagg tttgggagac aagaag 656  
                   --1.8 kb--

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Fig. 6-3

EXON 8	gctattccat	gccttctctt	tgtatttgg	tatgagactg	tagtttacag	ttcttttttgg	060	
	gannagagta	gaagagggat	gCAAAAACCTA	ATATTAGTAC	ATAATTTGTA	GTAGATATGG	120	
	ATGAAATTGT	TATCCTTCTA	ATGAAACCTA	ATAAGTAAAA	GTAGTAGAAT	GTTACCAAGA	180	
	TTATTTTGA	CCTAAGTTAT	AGTTAGAATA	CTTCATTATT	TTATATGATG	GATGTACAAT	240	
	TGTTCTTATC	TAATTTACCA	CTTTTACAGA	AACAGCTGTT	ATACCCATTA	ATGGTTCACC	300	
			y	sThrAlaVal	IleProIleA	snGlySerPr	(250)	
	TCGAACACCC	AGGCGAGGTC	AGAACAGGAG	TGCACGGATA	GCAAAACAAC	TAGAAAATGA	360	
	oArgThrPro	ArgArgGlyG	lnAsnArgSe	rAlaArgIle	AlaLysGlnL	euGluAsnAs	(270)	
	TACAAGAATT	ATTGAAGTTC	TCTGTAAAGA	ACATGAATGT	AATATAGATG	AGGTAATTTA	420	
	pThrArgIle	IleGluValL	euCysLysGl	uHisGluCys	AsnIleAspG	lu	(287)	
	ACTTCATGAT	TTCTTTAAAA	CAGTTAAAGT	AGATTTAGAT	GTAAGTTCTC	CCTAACAAATA	480	
	TTTACTTCTT	TTGTTATGAG	CATGTTTTTT	TTGTAATTAG	TGCTAACTCT	TTTGCAGTAG	540	
	CAAAATATTT	AGAAAAAtta	attcgttata	tttagttact	ttgatttaag	agagtagctc	600	
	cctcactct						609	
EXON 9				--1.8 kb--				
	aagcattgaa	gctgtaatgc	atgtgattgc	acctgtgaat	agccactaca	cttcagccta	060	
	ggcaatatag	agagaccctt	tctcTAAGAA	AATAATAAAA	AATAAAAAAG	TTATACACAG	120	
	ATTTTTTACT	GCATGGGGGA	TTGACACCTC	TAACCTACCC	TGCATTGTTC	AAGAGTCAAG	180	
	AGATTAGATT	TTGTTTTTAA	TTTTAATGAT	CATGTTGTAA	CTTCATCTTT	TTCAGGTGAA	240	
						VallY	(289)	
	<u>EcoRI</u>	AAATGTTTAT	TTCAAAAATT	TTATACCTTT	TATGAATTCT	CTTGGACTTG	TAACATCTAA	300
	sAsnValTyr	PheLysAsnP	heIleProPh	eMetAsnSer	LeuGlyLeuV	alThrSerAs	(309)	
	TGGACTTCCA	GAGGTAATCT	GAAAGGAAAT	TTAATAAAAT	ATTAATGTTT	TGAGACTGTG	360	
	nGlyLeuPro	Glu					(313)	
	GAGGGAGGAT	AATTGTCTAA	CTTTCTTAGA	TCAATTTACT	GTGTATCACA	TTTTTTTTTT	420	
	GCCCAAGAAG	AATCTAGCCA	AGTAGAATTG	TGGTGAAACT	AACCTTTTGT	TAGTAacaaa	480	
	<u>aagctt</u>						486	
EXON 10				--1.9 kb--				
	gtagcattgg	ctatctttgt	ctacataaaa	ttctaataaa	tattttctat	gcacgAAATA	060	
	GACCTAAAAAT	CAAAGTTGAA	CAAATGTTGC	AATTTTCTGT	ACCTCACTTT	TAGATAGACC	120	
	TTATTTATAT	TGCATGCGAA	CTCAGTGTAT	ATTACAAAAT	TAAATGTATA	TTATACAAAA	180	
	ATTCTTTAAT	GAAATCTGTG	CCTCTGTGTG	CTGAGAGATG	TAATGACATG	TAAAGGATAA	240	
	TTGTCAGTGA	CTTTTTTCTT	TCAAGGTTGA	AAATCTTTCT	AAACGATACG	AAGAAATTTA	300	
			ValGl	uAsnLeuSer	LysArgTyrG	luGluIleTy	(325)	
	TCTTAAAAAT	AAAGATCTAG	ATGCAAGATT	ATTTTGGAT	CATGATAAAA	CTCTTCAGAC	360	
	rLeuLysAsn	LysAspLeuA	spAlaArgLe	uPheLeuAsp	HisAspLysT	hrLeuGlnTh	(345)	
	TGATTCTATA	GACAGGTATT	GCACATGGTA	TATTTGATTG	ATTTGCTTTA	GATATAGGTT	420	
	rAspSerIle	AspSe				(350)		
	GATACTGATA	TAGGTAGATT	ATATAGTCTT	TAGCTTAGTG	ACCTTTAGAT	ATCATTTTATA	480	
	ACAAATTACT	TTCAAATGTC	TTTATACAAA	GAAAAGTTTA	ACAGTATTTT	AAGcatataa	540	
	cttatctaca	aatatagatt	taatgtgaat	tgtgtgtcct	ataacagtta	ccttttttnca	600	
	gttaactgaa	tataattttt	aaaatgtgca	ccaaaagata	atggcta		647	
				--1.0 kb--				

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Fig. 6-4

EXON 11	aataactgaac	aacttggtta	tcaataccnc	cagggagaag	catctgactt	tcacttttaa	060
	aaaaagactt	aatgattggt	atacctcttt	gtcataaaca	taatggaaag	agaccacaaa	120
	ttaaaaagng	tagtgAAAGG	TATTTTATTT	AAGCAGCAGC	TGGGTCATCT	ATTTTCTATC	180
	CTATCTATTA	TTGAGTTATC	ATTTTATATG	ATTTTATGAG	ACAACAGAAG	CATTATACTG	240
	CTTTTGTGAT	GCATAAAGCA	CAAATTGTA	ATTTTCAGTA	TGTGAATGAC	TTCATTATT	300
	GTTATTTAGT	TTTGAAACAC	AGAGAACACC	ACGAAAAAGT	AACCTTGATG	AAGAGGTGAA	360
		r PheGluThrG	lnArgThrPr	oArgLysSer	AsnLeuAspG	luGluValAs	(367)
	TGTAATTCCT	CCACACACTC	CAGTTAGGTA	TGAATTTTCC	TACTTTTAAT	TATATTATAA	420
	nValIlePro	ProHisThrP	roValAr				(326)
	TTTTGTTATT	CATGGCTTTA	TAGTGTTC	GATTTGTTCA	CGTTTCTTTA	TGTATTTCATA	480
	CATACATGTA	AGAAATATAT	ATTGAAGGCC	AGGTGTGGTG	GATCACACCT	GTAATCCAG	540
	CACTTTGGGA	GGCCAAGGCG	GGCAGATCAC	CTGAGGTTAG	GAGTTTGaga	ccggcctggc	600
	caacatggtg	aaaccccgtc	tctactagaa	atacaaaaat	tagctggggg	tgggtgggtg	660
	tgccgtgaat	ccagctgctc					680
	--3.2 kb--						
EXON 12	caataccatt	ttgttgccag	ttatatagtt	ctcctaaaaa	taatgccACT	ATTTTATTGA	060
	TATGTAGTTT	TATTAGTAAA	TAAGTATATC	TGTTCTATAA	CTATAAACTT	ATTGATTGTG	120
	AATACATATT	TTCTTAAAGA	TTTAAGTAAA	ATGTAATTTT	TTATAAACCA	CAGTCTTATT	180
	TGAGGGAATG	TAGAGACAAG	TGGGAGGCAG	TGTATTTGAA	GATACATTTA	ACTTGGGAGA	240
	TTGAAAACAT	TTCATTTTTT	CTTTTTTTCT	CCCTTCATTG	CTTAACACAT	TTTCTATTT	300
	TTATCCCCTC	TAGGACTGTT	ATGAACACTA	TCCAACAATT	AATGATGATT	TAAATTCAG	360
		gThrVal	MetAsnThrI	leGlnGlnLe	uMetMetIle	LeuAsnSerA	(392)
	CAAGTGATCA	ACCTTCAGAA	AATCTGATTT	CCTATTTTAA	CGTAAGCCAT	ATATGAAACA	420
	laSerAspG1	nProSerGlu	AsnLeuIleS	erTyrPheAs	n		(405)
	TTATTTTATTG	TAATATCTTG	GCAAAGAAAC	TTGAAATTAA	AAGTTAAAGT	ACTGACTTCT	480
	TTTTTAAATA	CTAATCTCCT	ATCTAACATG	TAGTTATCCA	TAATCTTTTC	TTGCTTTTTT	540
	AATCTTACAA	ATTATATATT	ATTAGTAGTA	TTGTTTTATT	TATACAGTGT	TATTTAAAC	600
	ATTTTATGT	TTACCTATTT	GCCTTgetca	ccattcttcc	ttcgaactta	tgccctcaqtt	660
	ctgagataat	tttttcttct	tcagatatat	cctttgataa	ttac		704
	--3.1 kb--						
EXON 13	aaaatttaga	taatagggtt	ttttagttgt	actgtagtat	tttttgctcg	attaacatcc	060
	AGTGAATGA	TATTGCTCTG	TTATGTTTCT	TAGTTGTGGT	TACCTAGTTA	TTATGGAAGT	120
	GTTCCACAT	TTTTATGAAC	AATTTAAAAA	GTCATATATT	ATGGAGCAGA	AAATATTAAT	180
	TCTGATTACA	CAGTATCCTC	GACATTGATT	TCTGTTTTTA	CCTCCTAAAG	AACTGCAGAG	240
					AsnCysThrV		(409)
	TGAATCCAAA	AGAAAGTATA	CTGAAAAGAG	TGAAGGATAT	AGGATACATC	TTTAAAGAGA	300
	alAsnProLy	sGluSerIle	LeuLysArgV	alLysAspI1	eGlyTyrIle	PheLysGluL	(429)
	AATTTGCTAA	AGCTGTGGGA	CAGGGTTGTG	TCGAAATTGG	ATCACAGGTA	ACTTGAATTC	360
	ysPheAlaLy	sAlaValGly	GlnGlyCysV	alGluIleG1	ySerGln		(444)
	ATTGTAATTC	GTGGTACTAT	AGAGTAATAA	TATTAAGAGC	AGCATCTTTC	CAGTTCGTAT	420
	AAATACTCTA	ACAGTATTTG	TCTAGTAGTA	TAAATACTG	TCAGATACTA	TATCCCTGCT	480
	GCCTGTGTAT	GCTGCTATTT	ATGGGAACTT	TATGGAAAAC	TACCTCCCAc	cccattataa	540
	aaactatgta	ataaaggaac	acatagccat	tgtagaaatt	ttng		584
	--1.8 kb--						
EcoRI							

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EXON 14	gaatgttaat	caccacttaa	tacttaagtt	gtgagtttta	gacaagctng	cttttgtggt	060
	gtcttggcgg	ccatatttgt	aagaagggtg	AGAAGTATGT	TTTAAGAAAA	GGCTTTTAA	120
	AAAATTTTAG	TAATTGTCAG	CTGGGTATAG	TGGTACATGC	CTATAATCCC	AGCCTCTTGG	180
	GAGGCCAAAG	CAGGAGGATC	TCTTGAGCCC	AGGAGTGTGA	AGGCCAGCCT	GGGCAAAACA	240
	GTGAGACTCC	ATCTCAAAAA	AAAAAAAAAA	TTTCATAATT	GTGATTTTCT	AAAATAGCAG	300
	GCTCTTATTT	TTCTTTTGT	TTGTTTGTAG	CGATACAAAC	TTGGAGTTCC	CTTGATTAC	360
				ArgTyrLysL	euGlyValAr	gLeuTyrTyr	(454)
	CGAGTAATGG	AATCCATGCT	TAAATCAGTA	AGTTAAAAAC	AATAATAAAA	AAATTTTCANC	420
	ArgValMetG	luSerMetLe	uLysSer				(463)
	CGGGCGCGGT	GGCTCACGCC	TGCAATCCCA	GCACTTTGGG	AGGCCGAGGT	GGGCAGATCA	480
EXON 15	GGAGGTCAAG	GCATCAAGAT	CATCCTGGCC	AAAATGGTGA	AACCCTGTCT	CTACTAAAAG	540
	TACAAAAATT	AGCTGGGCGT	GGTGGTGTAG	ACCTGTAGTC	CCAGCTACTT	GGCAGGCTGA	600
	GGCAGGAGAA	TCCCTTGAAC	CACGGAGGTG	GAGGTTCAG	TGAGCCAAGA	TTGTGCCATT	660
	TCACCCAGC	CTGGCAACAG	AGCAAGACAC	CATCTAAAAA	AAAAAAAAAA	AAAAAAAAAA	720
	ATTCAATGCT	GACACAAATA	AGGTTTCAAT	TAAACAACCT	CTTTTTTTTT	TTTAAATTA	780
	TCTGTTTCAG	GAAGAAGAAC	GATTATCCAT	TCAAAATTTT	AGGTAAATTT	TTTACTTTTA	840
		GluGluGluA	rgLeuSerIl	eGlnAsnPhe	Se		(474)
	GTAAAAAATT	TTTTTCTTTT	TATAGAAGTA	AGTATTTTAT	AATCTTTTTT	TTTTTCCTTT	900
	AGCAAACCTC	TGAATGACAA	CATTTTTCAT	ATGTCTTTAT	TGGCGTGCGC	TCTTGAGGTT	960
	rLysLeuL	euAsnAspAs	nIlePheHis	MetSerLeuL	euAlaCysAl	aLeuGluVal	(493)
EXON 16	GTAATGGCCA	CATATAGCAG	TAAGTTAAAT	TTTCATAAAT	AAACACTTTT	GTTCAATTTA	1020
	ValMetAlaT	hrTyrSerA					(500)
	AAGTTAAAA	GTGGTGTGTT	TCTTTGGTCG	GGGGAGAGGG	ATAGTGTGAG	GTAAAGGAGA	1080
	AGGAATGCTT	ATTTTAGATC	ACTATATACT	GAAGAATGTA	ATTGGTCATT	ATAAGCCATT	1140
	TAAGAGGCTT	ATTTGAGTTA	TTTGAggcca	tcttggggat	aatatttcac	taggettctc	1200
	ttctgagtat	actggtatac	tgaatccaaa	aaaggtactt	tttcgaaatc	cctccgaaga	1260
	cctttgagat	tgtagagtgc					1280
			--1.0 kb--				
	ggtattttaa	tctttgaaaa	tttgagatca	gctataagtc	ctttctctag	gaaaaacaca	060
	gaTTTGCATA	CACTCAAAAT	TGGAAGGCTA	TTTCCTATGA	GTCCGTAGAC	TCCAAAATAA	120
EXON 17	AAAATTTCTGC	TCTAAATAAA	AATGGTTTAA	CCTTTCTACT	GTTTTCTTTG	TCTGATAATA	180
	ACTTCCAAAA	AAATACCTAG	CTCAAGGGTT	AATATTTTCT	AAATAGTTAC	TTTTTTTTTT	240
	CATTTTTTAGG	AAGTACATCT	CAGAATCTTG	ATTCTGGAAC	AGATTGTGCT	TTCCCATGGA	300
	r	gSerThrSer	GlnAsnLeuA	spSerGlyTh	rAspLeuSer	PheProTrpI	(517)
	TTCTGAATGT	GCTTAATTTA	AAAGCCTTTG	ATTTTACAA	AGTGATCGAA	AGTTTATCA	360
	leLeuAsnVa	lLeuAsnLeu	LysAlaPheA	spPheTyrLy	sValIleGlu	SerPheIleL	(537)
	AAGCAGAAGG	CAACTTGACA	AGAGAAATGA	TAAACATTTT	AGAACGATGT	GAACATCGAA	420
	ysAlaGluGl	yAsnLeuThr	ArgGluMetI	leLysHisLe	uGluArgCys	GluHisArgI	(557)
	TCATGGAATC	CCTTGCATGG	CTCTCAGTAA	GTAGCTAAAT	AATTGAAGAA	ATTCAATTCAT	480
	leMetGlySe	rLeuAlaTrp	LeuSer				(565)
	GTGCATATGG	CTAACAAATT	ATTGTTAGTG	AGAGGTGTTT	CTTAACAAAT	CTACCTCAAG	540
	AACAAATAGG	GAATTTAATG	AATAATGTTA	TTTCAGTCTA	TAGCCCAAGG	ATCAagtgga	600
	atattagaat	ggagctttta	tcgagcacc	taaaccatct	aatacagcnc	agtgatttat	660
	ttaagaatag	cttttcttaa	aacatgccac	ttt			693
			--70.0 kb--				

EXON 18	at t t t t c t a a t	a t a a g c g t t g	a a g g t t a t a c	a t t t t t c t a c	t t t t t t g t g t	g t g g g a a g t a	060
	c a a a a a t t g t	C A A T T G G G A A	T T T C G A A G T A	G A G A A A A A T A	T T T C A T T C T G	A C T T T T A A A T	120
	T G C C A C T G T C	A A T T G T G C C T	A A A A T T C A T A	G T A C T T A C C A	T G T C A A A C A A	T A T G A T T T T G	180
	A T A T G T A C C T	G G G A A A A T T A	T G C T T A C T A A	T G T G G T T T T A	A T T T C A T C A T	G T T T C A T A T A	240
	G G A T T C A C C T	T T A T T T G A T C	T T A T T A A A C A	A T C A A A G G A C	C G A G A A G G A C	C A A C T G A T C A	300
	AspSerPro	LeuPheAspL	euIleLysG1	nSerLysAsp	ArgGluGlyP	roThrAspHi	(585)
	C C T T G A A T C T	G C T T G T C C T C	T T A A T C T T C C	T C T C C A G A A T	A A T C A C A C T G	C A G C A G A T A T	360
	sLeuGluSer	AlaCysProL	euAsnLeuPr	oLeuGlnAsn	AsnHisThrA	laAlaAspMe	(605)
	G T A A G G A A A A	T A T A T G T T A T	G T T G A C C A T C	A A A C T G C A A A	T A G A T T T T A A	G C A T A A G T G C	420
	A A T G T A A C A T	T C A T A A A A G A	V T T G T A G G G	A A T A G A A T T T	T G A A T A A G A	T A G T T T C T G T	480
	T T T T A A G A A A	T T A G T A A T A A	A A G G T A C A T g	a c c c a a a t a a	a g t c a t a t a a	a a g a g t a c a g	540
	a g t g c t a c t g	a a t c a c c t a g	g a t t t g c a t a	a t g a g a g c a g	t t t t c a t g g		589
	--3.0 kb--						
EXON 19	t g t t t t t a a g	c t g g a a t c a c	c t t a t g g t c t	c a a t a c c a c t	a t a a t t a t t a	a a a t t g T A C A	060
	T T A T A C A T A T	A T A G C T A T T T	T T T T C T A A T A	A G G C A G T A A T	C C C C A G G A A A	A G C C A T T T A T	120
	T A A A A T A G A A	T T A G A T A T G A	T G A T G A C A A G	C A G T T T T C C T	A T T A A T A T A T	C T T T C C C A G C	180
	T T G C A T T T A A	A T A G T C T G C T	A T A A T A C C A A	T T A A A T A G A C	A A G A T G T A T C	T G G G T G T A C A	240
	A C C T T G A A G T	G T A T G T A T A A	T C T G T G A T T C	T T A G C C A A C T	T G A A A T G A A G	A C T T T T C C T T	300
	T A A A T A T A T C	T A G G T A T C T T	T C T C C T G T A A	G A T C T C C A A A	G A A A A A A G G T	T C A A C T A C G C	360
		tTyrLeu	SerProValA	rgSerProLy	sLysLysGly	SerThrThrA	(621)
	G T G T A A A T T C	T A C T G C A A A T	G C A G A G A C A C	A A G C A A C C T C	A G C C T T C C A G	A C C C A G A A G C	420
	rgValAsnSe	rThrAlaAsn	AlaGluThrG	lnAlaThrSe	rAlaPheGln	ThrGlnLysP	(641)
	C A T T G A A A T C	T A C C T C T C T T	T C A C T G T T T T	A T A A A A A A G G	T T A G T A G A T G	A T T A T T T T C A	480
	roLeuLysSe	rThrSerLeu	SerLeuPheT	yrLysLysV			(654)
	A G A G C A T G G A	C T C T G A A A C T	A G G C T G A C T G	G G T T C A A A T C	A T G T T T C T T C	T A C T T T C T A G	540
	G T A C A T T A C T	G G G C A A G T C A	C T T A A T A T C T	C T G T G T C T C A	G T T T C C T c a t	c t a t a a a a t g	600
	g a a a t g a t a a	t g t t g c g a g a	t c t t t t c t t g a	c t a t t c a g a g	t c g t t t t c t g		650
EXON 20	--2.8 kb--						
	a a g g a a a a t c	c a t g c c c c n t	c g g g a c a t g c	c t g n c c t c t g	c a t t t c t t c a	t c t g t a t c c c	060
	t t g t a a t a t g	c c t c a t a a t a	a a c c a g t a a a	c a t G T T T C T C	T G G G G G A A A G	A A A A G A G T G G	120
	T A G A A A A G A G	G T T T C T G T T A	A A A T G C T A C T	T A A C A G C A T T	A T A A T T A G T G	T A A T T T C A T G	180
	A T T T G A A A A A	A A T C T A C T T G	T A A T T C A A A A	T G A A C A G T A A	A A A T G A C T A A	T T T T T C T T A T	240
	T C C C A C A G T G	T A T C G G C T A G	C C T A T C T C C G	G C T A A A T A C A	C T T T G T G A A C	G C C T C T G T C	300
		al TyrArgLeuA	laTyrLeuAr	gLeuAsnThr	LeuCysGluA	rgLeuLeuSe	(671)
	T G A G C A C C C A	G A A T T A G A A C	A T A T C A T C T G	G A C C C T T T T C	C A G C A C A C C C	T G C A G A A T G A	360
	rGluHisPro	GluLeuGluH	isIleIleTr	pThrLeuPhe	GlnHisThrL	euGlnAsnG1	(691)
	G T A T G A A C T C	A T G A G A G A C A	G G C A T T T G G A	C C A A G T A A G A	A A A T C A A G C A	C T T C A C C T T C	420
	uTyrGluLeu	MetArgAspA	rgHisLeuAs	pGln			(702)
	T C T C C T C C C T	A C T T A C T T G T	T A A C T G A T T T	C T T T C T T T C T	T T C T T T C T T T	C T T T C T T T C T	480
	T T C T T T C T T T	C T T T C T T T C T	T T C T T T T C T T	T C T T T T C T T T	C T T T C T T T C T	T T C C T T T T T T	540
	T T T T T T T G A G	A T A G A G T C T C	A C T C T G T T A C	C C A G G C T G G A	G T G C A G T G G C	G C A A T C T C G G	600
	C T C A C T G C A A	C C T C C G C C T C	C C A G G T C A A G	T G A T T C T C C T	G C C T C A G C C T	c c n a g g a g c t	660
	a g g a t a c a g g	c g t g t a c c a c	c a c a c c t t g t	t a a t t t t t g t	t a t t t a g t a g	a g a c a g g	717
	--4.0 kb--						

Fig. 8-7

	caagagccaa	agttagggtg	atttacaac	cagggtgatca	gtcctggata	attgagcctt	060
	ggtgatttgC	ATTTTGTCT	TTAAACACAC	TTTGGGTAA	ACACTTCATG	TAGACTTTCA	120
<u>SacI</u>	AACTGAGCTC	AGTATGGAAA	GAAATAACTC	TGTAGATTAA	ACCTTCTTT	TTTGAGGCTA	180
	AAAGAAAGAA	AATGGTATTT	TTTAAGAACA	AAACCATGTA	ATAAAATTCT	GACTACTTTT	240
EXON 21	ACATCAATTT	ATTTACTAGA	TTATGATGTG	TTCCATGTAT	GGCATATGCA	AAGTGAAGAA	300
		I	leMetMetCy	sSerMetTyr	GlyIleCysL	ysValLysAs	(716)
	TATAGACCTT	AAATTCAAAA	TCATTGTAAC	AGCATACAAG	GATCTTCCTC	ATGCTGTTCA	360
	nIleAspLeu	LysPheLysI	leIleValTh	rAlaTyrLys	AspLeuProH	isAlaValGl	(736)
	GGAGGTAGGT	AATTTTCCAT	AGTAAGTTTT	TTTGATAAAT	CCATATCCAT	AACATAACAT	420
	nGlu						(737)
	AGGTAATTCA	TTTGATCTCA	TTTATCATT	ATGAGATCAT	ATATTCTGTC	TGACCTTATT	480
	ATGTAAATTC	ACAAATAAAA	ACTTTTATAT	TATTTATTTG	TAACTTAAAT	AGAATTGGAA	540
	AGATAAGGGT	AATTATGAAA	TTACCCATAT	CATAGTTTTT	TATAAAGTTA	ATAAATAATA	600
	TTTTATCCCT	GTAATAAGCA	GGTATTGTa	ataaacttga	catgagtcac	agaacattag	660
	atatcttgag						670
				--0.2 kb--			
<u>XbaI</u>	tccatctgct	gctgcectgc	tatttctctc	aatcgattct	gtgacatttc	acttctagaa	060
	gagcaGCTAT	AATCCAAGCC	TAAGAAGTAA	TTTTATTTAT	TTATTATTTT	TTCTTTTATA	120
	ATATGTGCTT	CTTACCAGTC	AAAAAGTATT	ATAAACTATT	AGAAAAGAAA	ATCTAAAGGT	180
EXON 22	AGAAATTTTA	AAATTCATTT	AACAAGTAAA	TTTTACTTTT	TTTTTTTTTT	TTTTTTTTTT	240
	ACTGTTCTTC	CTCAGACATT	CAAACGTGTT	TTGATCAAAG	AAGAGGAGTA	TGATTCTATT	300
		ThrPh	eLysArgVal	LeuIleLysG	luGluGluTy	rAspSerIle	(752)
	ATAGTATTCT	ATAACTCGGT	CTTCATGCAG	AGACTGAAAA	CAAATATTTT	GCAGTATGCT	360
	IleValPheT	yrAsnSerVa	lPheMetGln	ArgLeuLysT	hrAsnIleLe	uGlnTyrAla	(772)
	TCCACCAGGG	TAGGTCAAAA	GTATCCTTTG	ATTGGAAAAA	TCTAATGTAA	TGGGTCCACC	420
EXON 23	SerThrArg						(775)
	AAAACATTAA	ATAAATAATC	TACTTTTTTG	TTTTTGCTCT	AGCCCCCTAC	CTTGTCACCA	480
					ProProTh	rLeuSerPro	(781)
	ATACCTCACA	TTCTCGAAG	CCCTTACAAG	TTTCCTAGTT	CACCCCTTACG	GATTCCTGGA	540
	IleProHisI	leProArgSe	rProTyrLys	PheProSerS	erProLeuAr	gIleProGly	(801)
	GGGAACATCT	ATATTTTACC	CCTGAAGAGT	CCATATAAAA	TTTCAGAAGG	TCTGCCAACA	600
	GlyAsnIleT	yrIleSerPr	oLeuLysSer	ProTyrLysI	leSerGluGl	yLeuProThr	(821)
	CCAACAAAAA	TGACTCCAAG	ATCAAGGTGT	GTGTTTTCTC	TTTAGGGAAG	TAGTAAAGAA	660
	ProThrLysM	etThrProAr	gSerAr				(830)
	TGAGAGGGGG	ATTATTTTGA	TCCAAGAATA	AAAAATATAA	AGCATTCTTC	ATTTCAAATA	720
	AGCTAGACTC	TTGAACTCT	ATTTGCTTAT	TTAAGTAACA	TAATAAGAAT	ATGGGGGCGG	780
	GGTGAAGAAA	ATCTATTTAC	GACTTAAGCA	ACGCAAGATG	GCCGAATAGG	AACAGCTCCg	840
	gtctacagct	cccagcgtga	gcacgcagaa	gacgggtgat	ttctgcattt	ccatctgagg	900
	taccgggttc	atctcactag	ggagtgccag	acagt			935
				--7.4 kb--			
	ttgataactt	accattgat	ttatgaagaa	ctaagtaggg	gtaaccttga	aacttgccctt	060
	tgccctccct	aaatatgggc	aatggcagna	tatgttcttg	cagacctata	acttttgcTT	120
	TAAACTAAG	AGACTAGGTG	AGTATATGAT	TAGACGGGCA	CTGTTAGAAT	AATTCCCAAA	180
	TGAATATAGT	TTGTCAGTGG	TTCTAGGGTA	GAGGTAACCT	TTAATTTGGT	ATTCTAATA	240
EXON 24	GTTCAGAATG	ATGTATTTAT	GCTCATCTCT	GCAAAATTGT	ATATGGTTTT	TTATTACTAA	300
	TTGGTATTTT	ATCTTAACTT	GACAGAATCT	TAGTATCAAT	TGGTGAATCA	TTCGGGGTGA	360
			gIleL	euValSerIl	eGlyGluSer	PheGly	(840)
<u>HindIII</u>	GTATTTTCTT	TCTATGAAAT	ATAATAGTAT	GCATTGTAAG	TATAAAAGAA	ATTAAAGCTT	420
	TCTATAATTT	GAATTTCCAA	ATGCAGTTAT	TCAAACACCT	CATCCAGGCA	TATTGCATAG	480
	AATTTTATGA	GATATATATA	TCTCAGATTT	ACTTTCAAAT	CAAGTTTAAT	CTCAATCAT	540
	ACTCCTAATT	GGTGAACCTC	AAAACTTTTC	TAAATATCCA	CTTGAGATTA	TATAATACAT	600
	ATATACATTT	GTGTATATAC	ATACATATAT	ACGTGAGCTG	TTTTTGCTCA	CAACATTTCT	660
	ATCACCAAAT	GTGTGAGATT	TTTTTCTCAC	CCAAATCTAT	TCTTcaactc	tctgggtgctt	720
	ctacaattca	attcaattct	gacactaatt	acccagag			758
				--2.8 kb--			

09337158-033199

EcoRI  
EXON 25

EXON 26

EXON 27

HindIII

```

888gatggaa ttaggtagtt attctgattt ttAGATTTTT CATATCTTTT ATTTGGTCCA 060
ATGAAGCAGA AAATTTAAAT GAAGTTATTA CCTTTGCCTG ATTTTGGACA CACCTCAAAC 120
TATAACTTGA GGTGCTAAC TATGAAACAC TGGCATTAA TGATTTAAAG TAAAGAATTG 180
TGTAATTTGT AGACTTCTGA GAAGTTCCAG AAAATAAATC AGATGGTATG TAACAGCGAC 240
          ThrSerG1 uLysPheGln LysIleAsnG lnMetValCy sAsnSerAsp (856)
CGTGTGCTCA AAAGAAGTGC TGAAGGAAGC AACCCTCCTA AACCCTGAA AAACTACGC 300
ArgValLeuL ysArgSerAl aGluGlySer AsnProProL ysProLeuLy sLysLeuArg (876)
TTTGATATTG AAGGATCAGA TGAAGCAGAT GGAAGGTAGG AACCAGTTTT GAATGTTTTT 360
PheAspIleG luGlySerAs pGluAlaAsp GlySe. (888)
CAGTAGCTGA GATGGTCATC TGGGGAATCC AGAGTCTCAG CACTGCTCCT GGCTTATACC 420
AATTTCTTTC ATGCCAAGTT TATTTGGAAG TTGTGAGAAT GGCTCAAAT AATAGATATG 480
AGTGTAGTGC AAAGTTAAAA ACATCTTACA AATTGCATAC CAACATTGAG TGAAGATATC 540
TAATAAACCCT TGATCTTTTT TACAAAGCTA TTGATAAAAT TTTGTTATTC TTAACATTAA 600
ATTTAAAAAT GTTTACTCTT GAAAAATATT AACCCTGTA TTTTGTGAGA ACCACTGAAA 660
AAATACATAG CATCATAAAT TTGTGACATT TATGTTTTAG ATGGTTAGTT TTTAAATTTT 720
AAAATTAAAA GCTACTCACT AAAATAATAG CATAAAGTAA GTCATCGAAA GCATCATAGT 780
TACTGGAAAT TTGAGTTTTT CATTTATAAA TACACATGAA ATGTTTTGCA TTTTTTAAT 840
CTGCAGTAAA CATCTCCAG GAGAGTCCAA ATTTGAGCAG AAACCTGGCAG AAATGAGTAA 900
          rLys HisLeuProG lyGluSerLy sPheGlnGln LysLeuAlaG luMetT (905)
GTACTTTTTT CACCTTGTGT AAACGAAATA AACAAATGTT TACTGCGAA GAAGTCTTTT 960
CGTTATATAA AAGATGTAT AATTTCTTCA GTTGGCAGGT TTGTTTATGC ATTTAAAAATA 1020
TAATTCATC AAGGTATTT ATCTACAAAC ATTTGTGGAT TAAATGTATG ATGTAAAAATG 1080
AAGGTCATTT TTACCTTTT TATGATCTTT CATGCAGGAA GACTAAGAAG TGAACATTG 1140
CTTGACCACA TTCAAcacaa atggtacag ttagaaata ctttagcaga actacaaaga 1200
gggaactat tggagtggt gatataggg aaagttttat aaacctagca tatgtaaaac 1260
atcatcacc ttatttaagg aataaccttt gattctaccg atttttaaac 1310
          --1.7 kb--

tctagctatt tgaatatgca gtaaattaac tgtaaactct acggtactgt caaatactag 060
aatgaagacc acctettttt gcAAGGTCCT GAGCGCCATC AGTTTGACAT GACGATAATA 120
TATATGGCAG CCACTTGCCA ACTTACCCAG TACCATCAAT GCTGTTAACA GTTCTTCATC 180
CTTTTTCCAG CTTCTACTCG AACACGAATG CAAAAGCAGA AAATGAATGA TAGCATGGAT 240
          hrSerThrAr gThrArgMet GlnLysGlnL ysMetAsnAs pSerMetAsp (921)
ACCTCAAACA AGGAAGAGAA ATGAGGATCT CAGGACCTTG GTGGACACTG GTTACACCTC 300
ThrSerAsnL ysGluGluLy sEND 3' untranslated region begins here (928)
TGGATTCAAT GTCTCTCACA GATGTGACTG TATAACTTTC CCAGGTTCTG TTTATGGCCA 360
CATTTAATAT CTTCACTCTT TTTTGTGGAT ATAAATGTG CAGATGCAAT TGTTGGGTG 420
ATTCTAAGC CACTTGAAAT GTTAGTCATT GTTATTTATA CAAGATTGAA AATCTGTGT 480
AAATCCTGCC ATTTAAAAAG TTGTAGCAGA TTGTTTCCTC TTCCAAAGTA AAATGCTGT 540
GCTTTATGGA TAGTAAGAAT GGCCCTAGAG TGGGAGTCCT GATAACCCAG GCCTGTCTGA 600
CTACTTTGCC TTCTTTTGTA GCATATAGGT GATGTTTGCT CTTGTTTTTA TTAATTTATA 660
TGTATATTTT TTTAATTTAA CATGAACACC CTTAGAAAAT GTGTCTATC TATCTCCAA 720
ATGCAATTTG ATTGACTGCC CATTACCAA AATTATCCTG AACTCTTCTG CAAAATGGA 780
TATTATTAGA AATTAGAAAA AAATTACTAA TTTTACACAT TAGATTTTAT TTTACTATTG 840
GAATCTGATA TACTGTGTGC TTGTTTTATA AAATTTTGCT TTTAATTAAA TAAAAGCTGG 900
AAGCAAAGTA TAACCATATG ATACTATCAT ACTACTGAAA CAGATTTTAT ACCTCAGAAT 960
GTAAAAGAAC TTAAGTATTA TTTTCTTCAT CCAACTTATG TTTTAAATG AGGATTATTG 1020
ATAGTACTCT TGGTTTTTAT ACCATTGAGA TCACTGAATT TATAAAGTAC CCATCTAGTA 1080
CTTGAAAAAG TAAAGTGTTT TGCCAGATCT TAGGTATAGA GGACCCTAAC ACAGTATATC 1140
CCAAGTGCAC TTTCTAATGT TTCTGGGTCC TGAAGAATTA AGATACAAAT TAATTTTACT 1200
CCATAAACAG ACTGTTAATT ATAGGAGCCT TAATTTTTTT TTCATAGAGA TTTGTCTAAT 1260
TGCATCTCAA AATTATTCTG CCTCCTTAA TTTGGGAAGG TTTGTGTTTT CTCTGGAATG 1320
GTACATGTCT TCCATGTATC TTTTGAAGTG GCAATTGTCT ATTTATCTTT TATTTTTTTA 1380
AGTCAGTATG GTCTAACACT GGCATGTTCA AAGCCACATT ATTTCTAGTC CAAAATTACA 1440
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09387458-083490

EXON 27  
(CONTD)

TTCAAATTAA AACAGCTGCA TTAGAAAAAG AGGCGCTTCT CCCCTCCCCT ACACCTAAAG 1560  
 3' untranslated region (continued)  
 GTGTATTTAA ACTATCTTGT GTGATTAAC TATTTAGAGA TGCTGTAAC TAAAAAGGG 1620  
 GATATTTAAG GTAGCTTCAG CTAGCTTTTA GGAAAAATCAC TTTGTCTAAC TCAGAATTAT 1680  
 TTTTAAAAAG AAATCTGGTC TTGTTAGAAA AAAAAATTTT ATTTTGTGCT CATTAAAGTT 1740  
 TCAAACTTAC TATTTTGACA GTTATTTTGA TAACAATGAC ACTAGAAAAC TTGACTCCAT 1800  
 TTCATCATTG TTTCTGCATG AATATCATAC AAATCAGTTA GTTTTTAGGT CAAGGGCTTA 1860  
 CTATTTCTGG GTCTTTTGCT ACTAAGTTCA CATTAGAATT AGTGCCAGAA TTTTAGGAAC 1920  
 TTCAGAGATC GTGTATTGAG ATTTCTTAAA TAATGCTTCA GATATTATTG CTTTATTGCT 1980  
 TTTTGTATT GGTAAAACT GTACATTTAA AATTGCTATG TTAATTTT CTACAATTAA 2040  
 TAGTTTGTCT ATTTTAAAT AAATTAGTTG TTAAGAGTC TTAATGGTCTG ATGTTGTGTT 2100  
                   polyadenylation signal sequence                   polyadenylation site  
 CTTTGTATTA AGTACACTAA TGTTCTCTTT TCTGTCTAGG AGAAGATAGA TAGAAGATAA 2160  
 CTCTCCTAGT ATCTCATCCA TTCCTAGCCT TTAAGGGGCT CTATATGCTA GAGATTTCCA 2220  
 AATTTATTTT TTCAGCCCTG ATCTTTTCAC AGAGGTCAAG Gcttttatag ccaacagaac 2280  
 tcttgattcc tactccctc tacccaatgt ctccaaatat aaactaaaat caaataaata 2340  
 aaaatccttt tt ; 2352

09387158-083199

Fig. 7

# HUMAN RETINOBLASTOMA GENE

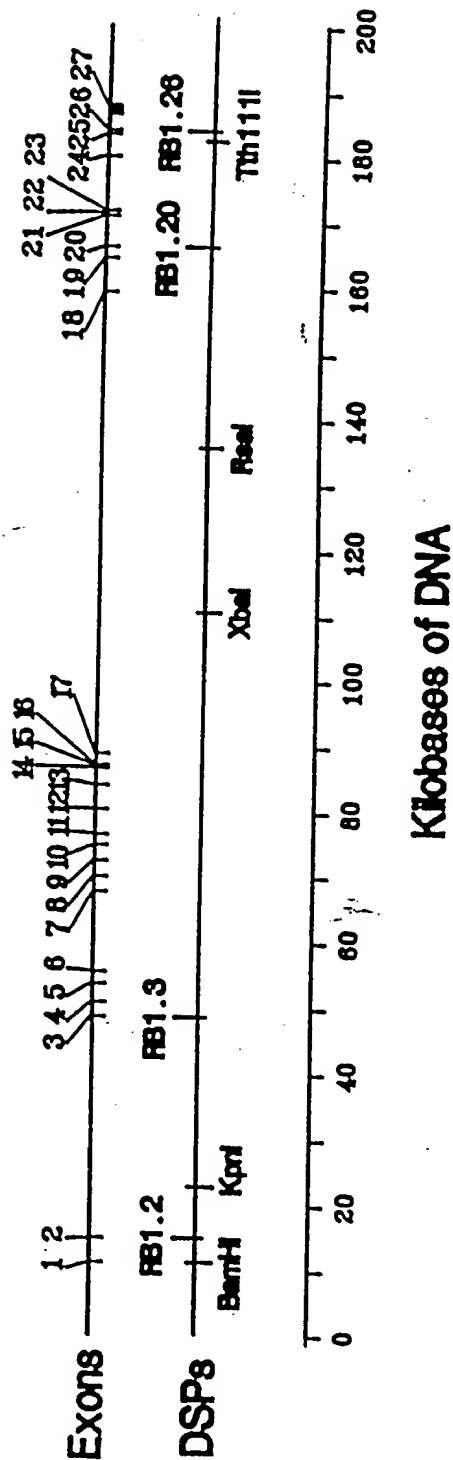




Figure 8

Fig. 8  
RB - 6

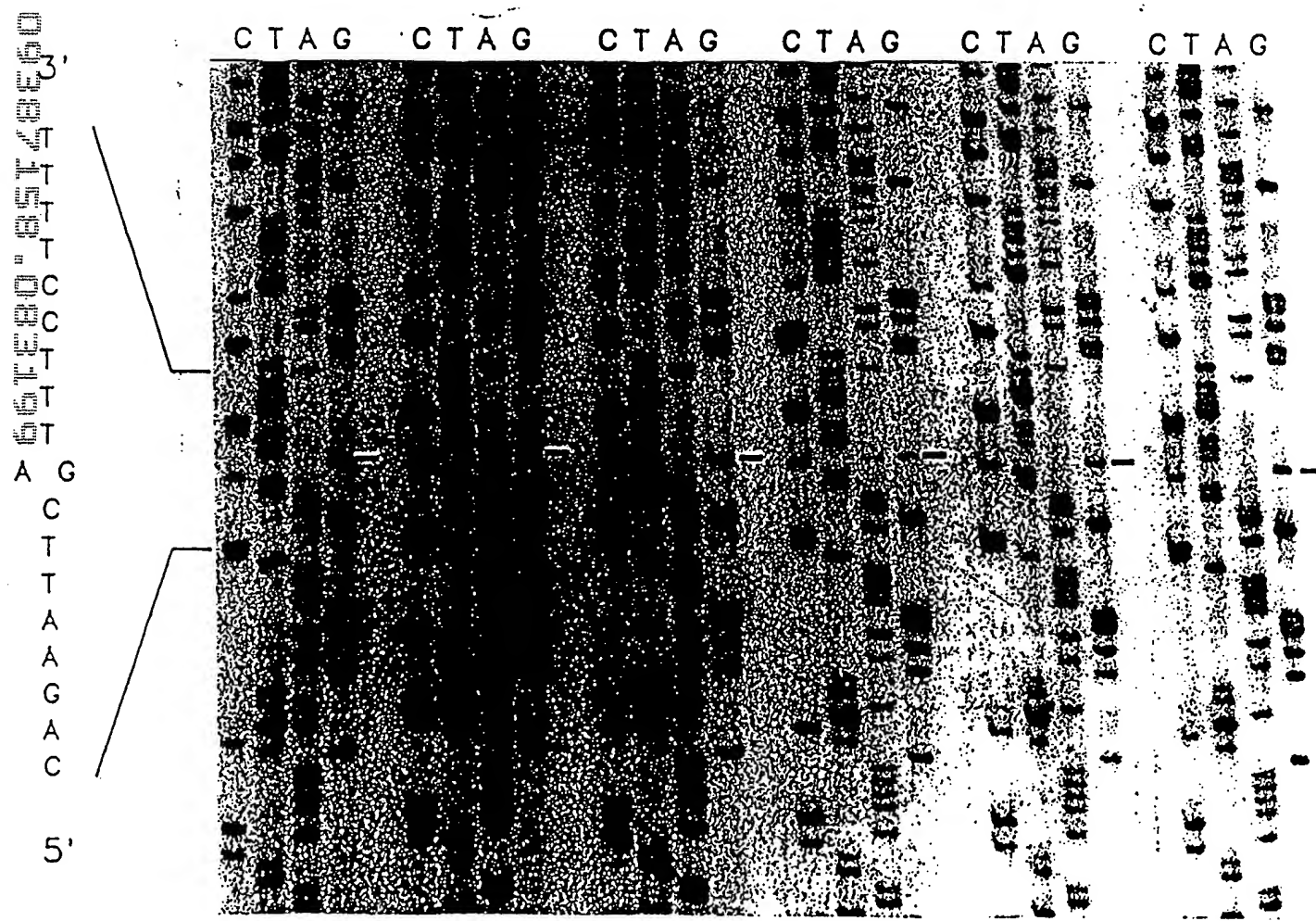
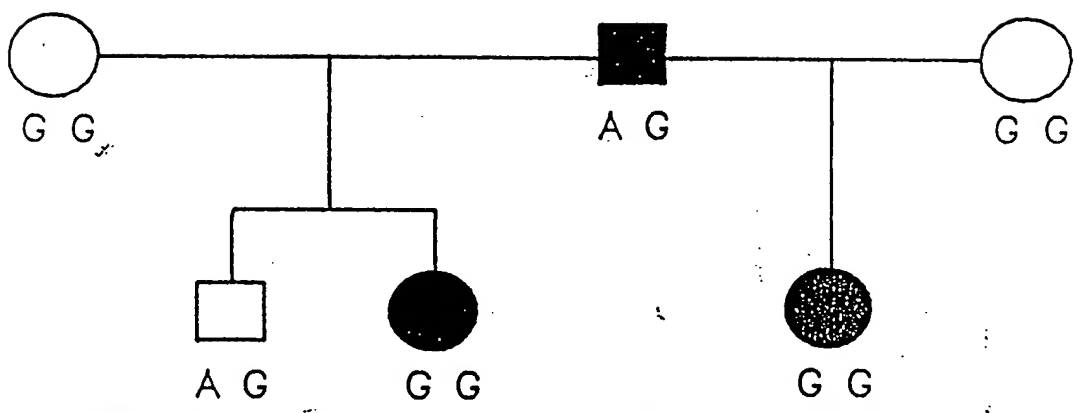
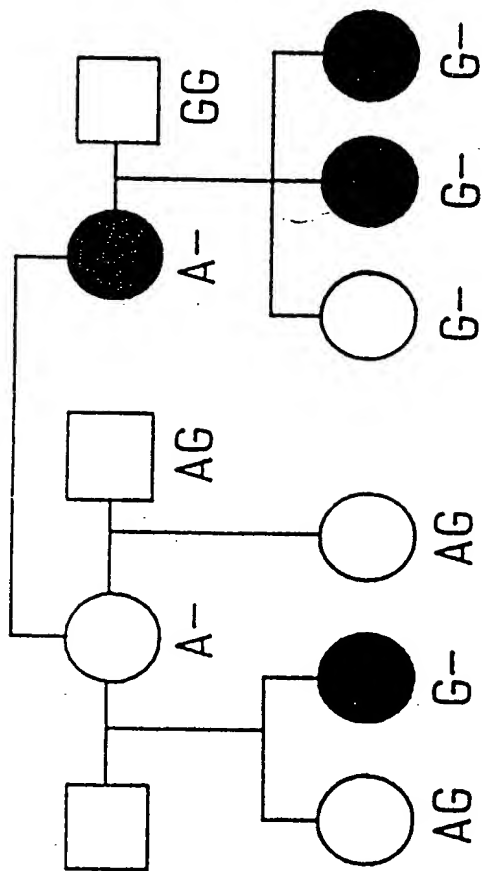
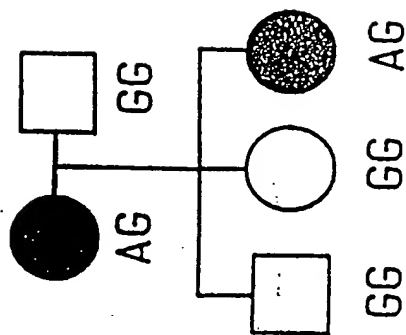


Fig. 9

RB-32



RB-36



RB-50

